

CLAIMS

What is claimed is:

1. A method of inducing transplant tolerance in a mammal, comprising inhibiting T-cell costimulation and IL-2 mediated T-cell proliferation without inhibiting IL-2 mediated T-cell apoptosis.
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2. A method of inducing transplant tolerance in a mammal, comprising administering to said mammal an effective dose of a T-cell costimulation blockade agent and an effective dose of an immunosuppressive agent, while maintaining normal levels of T-cell death.
- 10 3. The method of Claim 2 wherein the immunosuppressive agent is rapamycin, or a biologically active derivative thereof.
4. The method of Claim 2 wherein the costimulation blockade agent and the immunosuppressive agent are administered substantially simultaneously.
5. The method of Claim 2 wherein the costimulation blockade agent and the immunosuppressive agent are administered simultaneously and subsequently the immunosuppressive agent is administered continuously at effective doses.
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6. The method of Claim 2 wherein the costimulation blockade agent comprises at least one agent that blocks a signaling pathway mediated by CD40, CD40L, B7, CD28 or CTLA4.
- 20 7. The method of Claim 6 wherein the costimulation blockade agent comprises at least one agent selected from the group consisting of anti-CD40 antibodies, anti-

CD40L antibodies, anti-B7 antibodies, anti-CD28 antibodies, anti-CTLA4 antibodies, B7-Ig, CD28-Ig, CD40-Ig, CD40L-Ig, CTLA4-Ig, soluble extracellular domain proteins of CD40, CD40L, B7, CD28 and CTLA4 and derivatives thereof, and costimulation blockade drugs.

- 5 8. The method of Claim 2 wherein the costimulation blockade comprises anti-CD40L and CTLA4-Ig.
9. The method of Claim 3 wherein the rapamycin is contained in a fish oil composition.
- 10 10. The method of Claim 3 wherein the route of administration is intraperitoneal,
10 intravenous, oral or subcutaneous.
11. A composition comprising at least one costimulation blockade agent and rapamycin, or a biologically active derivative thereof.
12. The composition of Claim 11 further comprising fish oil.
13. The method of Claim 11 wherein the costimulation blockade agent comprises at
15 least one agent selected from the group consisting of anti-CD40 antibodies, anti-CD40L antibodies, anti-B7 antibodies, anti-CD28 antibodies, anti-CTLA4 antibodies, B7-Ig, CD28-Ig, CD40-Ig, CD40L-Ig, CTLA4-Ig; soluble extracellular domain proteins of CD40, CD40L, B7, CD28 and CTLA4 and derivatives thereof, and costimulation blockade drugs.
- 20 14. A kit comprising at least one costimulation blockade agent and rapamycin.

15. A method of inducing transplant tolerance in a mammal comprising administering a T-cell costimulation blockade agent, wherein T-cell proliferation, but not T-cell apoptosis is inhibited.
- 5 16. A method of inhibiting T-lymphocyte induced rejection of an allograft in a mammal comprising administering a T-cell costimulation blockade agent and an immunosuppressive agent, wherein T-cell costimulation and IL-2 mediated T-cell proliferation are inhibited and IL-2 mediated T-cell apoptosis is not inhibited.
- 10 17. The method of Claim 16 further comprising administering an effective dose of rapamycin or a derivative thereof.
18. A method of prolonging the survival of an allograft in a mammal, comprising administering a T-cell costimulation blockade agent and an immunosuppressive agent, wherein T-cell costimulation and IL-2 mediated T-cell proliferation are inhibited and IL-2 mediated T-cell apoptosis is not inhibited.
- 15 19. The method of Claim 18 further comprising administering an effective dose of rapamycin or a derivative thereof.
20. A method for inducing T-cell non-responsiveness to a donor tissue or organ in a recipient, comprising administering a T-cell costimulation blockade agent and an immunosuppressive agent, wherein T-cell costimulation and IL-2 mediated T-cell proliferation are inhibited and IL-2 mediated T-cell apoptosis is not inhibited.
- 20 21. The method of Claim 20 further comprising administering an effective dose of rapamycin or a derivative thereof.